Carboxyhemoglobin in Nonsmokers

A Mathematical Model

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A study was made of existing mathematical models for both carbon monoxide (CO) and carboxyhemoglobin (COHb) buildup. From these models a combined model was derived for calculating Δ%COHb in nonsmokers in an enclosed space in which excess concentrations of CO may occur. For simplicity the model was restricted to those occasions where CO concentration was at equilibrium or came to equilibrium in a time-short compared with exposure time.

The equation derived was for Δ%COHb calculated from CO, ventilation, respiration, persons, smokers, height, weight, cigarettes, and exposure time. Comparisons with published data show excellent agreement of calculated and observed values.

In recent months attention has been focused on a nonsmoker's exposure to various substances in the atmosphere.[1] Several studies have been made to determine the extent and effect of this exposure.[2-8] One compound, carbon monoxide (CO), is common to virtually all studies reported thus far. The principal reasons for the use of CO as a model for exposure are ease of atmospheric analysis, ease of physiologic analysis (COHb), stability of CO, extant data on mechanisms of uptake and release.

Of particular interest are the occasions when a nonsmoker is in a confined space. Examples of this situation would be an automobile, a plane, a bus, or a meeting room. Calculations have been made on the buildup of CO in confined spaces with employment of empirical equations.[3-5] Several equations have also been derived for the uptake of CO as carboxyhemoglobin (COHb).[9-12] This study examines existing mathematical expressions and derives a single expression that would permit the calculation of COHb change in a nonsmoker when in a confined space.

CARBON MONOXIDE BUILDUP

The most frequently used equation for vapor and gas buildup is Turk's equation as cited and used by Owens and Rossano.[3]

The equilibrium concentration of CO can be readily calculated from a simplification of that equation. The equation is:

$$C = \frac{CiQi + G}{Qi} \qquad (1)$$

Where:

C = equilibrium concentration of CO in mg/cu m

Ci = concentration in ventilating air in mg/cu m

Qi = rate of ventilation flow in cu m/min

G = rate of CO generation in space in mg/min.

Both the full equation and this simplified form have been tested for validity and found suitable for CO.[4-13]

The value of "G," the rate of generation in the space, depends on the number of people in the space and the number of cigarettes smoked per unit time, together with the generation rate per person and per cigarette. This leads to the following equation:

$$G = \frac{(Np \times 17.38) + (Ns \times Nc \times 74.0)}{60} \qquad (2)$$

Where:

Np = No. of persons in the space

Ns = No. of smokers in the space

Nc = No. of cigarettes/hr/smoker.

The constants for emission rates are taken from the data of Owens and Rossano[3] and Jones and Fagan.[13] Combining and simplifying (1) and (2) gives:

$$C = \frac{CiQi + 0.2897\ Np + 1.233\ NsNc}{Qi} \qquad (3)$$

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This is a general equation for the equilibrium concentration of CO in an enclosed space where body emissions and cigarettes are the only sources of CO other than the ventilation air.

CARBOXYHEMOGLOBIN BUILDUP

From Haldane's initial work in 1895,[14] several different equations have arisen. Rodkey et al[15] used current data to obtain %COHb saturation by the first law of Douglas et al.[16] Earlier Forbes et al[10] had worked out a nomograph for change in %COHb saturation. Recently Ramsey[9] successfully applied a relation derived by Pace et al.[17] Peterson and Stewart[11] and Stewart et al[12] have contributed extensions to cover the range up to 35,000 ppm CO, and intermittent exposures.

After consideration of all these equations, the one of Pace et al[17] was selected as being the most useful in the context of this study, based on its demonstrated applicability for low CO exposures[9] and its simplicity. The equation is as follows:

$$\Delta\%COHb = \frac{C \times V_r \times t}{46.5 \times V_b} \qquad (4)$$

Where:

C = CO concentration in parts per 10,000

V_r = minute volume of respiration, liter

V_b = total blood volume, liter

t = exposure time, min.

According to Pace et al[17] this equation is valid up to the point where the COHb concentration is one third the equilibrium value at the specified CO level. Beyond the one-third point, the rate of CO uptake decreases in a nonlinear fashion. Peterson and Stewart[11] and Stewart et al[12] have shown that a log-log relation is then obtained, therefore, equation (4) will tend to overestimate Δ%COHb at a concentration beyond one third of equilibrium.

In the search for data on blood volume and respiration rates, an equation for blood volume was found.[18] The equation related blood volume to height and weight as follows:

$$V_b = (46.6\,H + 21.6\,W - 4670)\,10^{-3} \qquad (5)$$

Where:

V_b = total blood volume, liter

H = height, cm

W = weight, kg

This equation is fairly representative of adult men and women. The same source gave the following as "representative" minute volumes[18]:

Rest, 7.43, liter

Light activity, 11.7, liter

Light work, 28.6, liter

Heavy work, 42.9, liter

These volumes are for an average man 68.5 kg in weight and 177.8 cm in height.

THE SYSTEM TO BE MODELED

Before attempting to construct a mathematical model, the system must be described. The system under consideration is the COHb change in nonsmokers in an enclosed space and in the presence of one or more persons smoking cigarettes. The parameters of the system that must be specified are CO concentration, time of exposure, and certain physical characteristics of the exposed individual(s). CO concentration is specified by another set of parameters dealing with the space and its occupancy, and ventilation. This set also includes a time factor. Combining the sets of parameters the following list is obtained.

Parameters Necessary to Estimate Δ%COHb

1. Space volume
2. Ventilation rate
3. Ventilating air CO concentration
4. Total occupancy of the space
5. No. of smokers
6. No. of cigarettes per smoker per unit time
7. Time since occupancy of space
8. Height of individual to be estimated
9. Weight of individual to be estimated
10. Minute respiratory volume
11. Time of exposure

Obviously most of these parameters are obtained easily or estimated. However, time appears twice with differing functional connotations and possibly differing zero points. The mathematics would be simplified greatly if one of these time factors could be eliminated.

CONSTRAINTS AND LIMITS ON THE SYSTEM

In the calculation of both CO and COHb, an equilibrium is involved. Calculations of CO buildup vs time show very little linearity until equilibrium is approached.[13] On the other hand, COHb buildup vs time (at constant CO level) shows a linear trend up to one third of the equilibrium value.[17] Consequently it would be simpler and more accurate to limit the considerations to times when the CO is at or near equilibrium and COHb is less than or equal to one third of equilibrium.

This limitation will permit consideration of those situations where equilibrium concentration of CO is reached in a time that is short compared with the exposure time. Or, alternatively, it would also permit examination of situations where exposure is initiated in a space already at equilibrium CO concentration. Under these circumstances the calculation of CO concentration is handled adequately by equation (3). That equation is independent of both time and volume.

For Δ%COHb the limitation imposes few restrictions. However, the dependence on minute respiratory volume could cause consideration to be limited to situations where the volume was less than that cited above for light activity. That would ensure reasonable times for values less than one third the equilibrium COHb concentration.

THE MODEL

The first model is equation (4). By substituting (5) in (4) the model is generalized in more easily measured parameters.

$$\Delta\%COHb = \frac{C \times V_r \times t \times 10^{-2}}{2.167\,H + 1.004\,W - 214.2} \qquad (6)$$

The 10^{-2} is included so that C is expressed in parts per million rather than the parts per 10,000 of equation (4). Equation (3) can now be substituted for C and multiplied by 0.8778 to express C in milligrams per cubic meter rather than parts per million.

$$\Delta\%COHb = \frac{CiQi + 0.2897\ Np + 1.233\ NsNc}{Qi} \times 0.8778 \times \frac{V_r \times t \times 10^{-3}}{2.167\ H + 1.004\ W - 217.2}$$

$$= \frac{(8.778\ CiQi + 2.543\ Np + 10.82\ NsNc)\ V_r\ t}{(2.167\ H + 1.004\ W + 217.2)\ Qi} \times 10^{-3} \qquad (7)$$

The parameters of this equation have the same units and designations as noted above, that is:

Ci = Concentration of CO in input air, mg/cu meter

Qi = Rate of input ventilation, cu meter/min

Np = No. of persons in the space

Ns = No. of smokers in the space

Nc = No. of cigarettes/hr/smoker

Vr = Minute volume of respiration, liter

t = Exposure time, min

H = Individual's height, cm

W = Individual's weight, kg

The following modification of the equation of Rodkey et al[15] is used to calculate the equilibrium value for COHb:

$$\%COHb = \frac{15.08\ C}{100.4 + 0.1508\ C} \qquad (8)$$

Where:

C = CO concentration in ppm

Possession of the equilibrium value of COHb permits estimation of the time at which linearity ceases to be a valid assumption in estimating Δ%COHb.

NUMERICAL RESULTS

Smoking in various locations, both public and private, has been a source of much discussion. The effects of CO have figured prominently in these discussions. The following cases show the application of equation (7) to several such situations.

Automobiles

The flow rates of ventilating air in a standard four-door American sedan can vary from about 1.42 cu m/min to about 6.51 cu m/min depending on driving speed and vents, heating or air-conditioning facilities in use. The small volume (ca 3 cu m) of the automobile will furnish a rapid CO equilibrium at the lowest of these flow rates and meet the restrictions set forth, that exposure time be much longer than the time to reach CO equilibrium. As a worst-case situation, the following parameters might be set:

Ambient CO = 17.7 mg/cu m
Ventilation = 1.42 cu m/min
Minute volume = 11.7 liter
No. of persons = 5
No. of smokers = 4
No. of cigarettes/person/hr = 3.5
Av height/person = 177.8 cm
Av weight/person = 68.5 kg

The ambient CO is approximately the average value for Chicago in 1964 to 1965.[16] The number of cigarettes is nearly three times that suggested by Owens and Rossano,[3] but is equal to a rate recently reported.[2] The minute volume assumes that the driver is the nonsmoker and that driving constitutes light activity. A plot of Δ%COHb vs time is shown in Fig 1. An exposure of two hours to this environment is calculated to cause a Δ%COHb of about 1.6%. Obviously, this is a relatively small increase. It reflects, however, the effect not only of smoking but also of the ambient CO. To isolate the effect of smoking

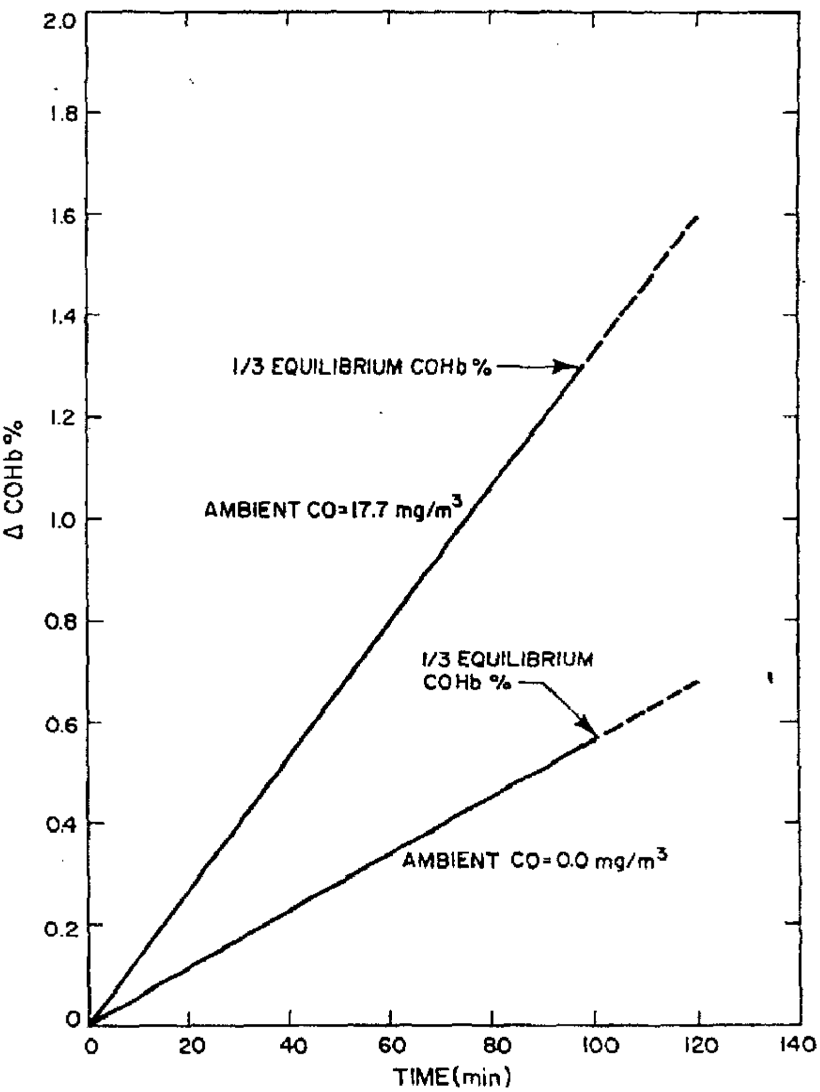

Fig 1.—Δ%COHb as a function of time for the driver of an automobile with four smoking passengers.

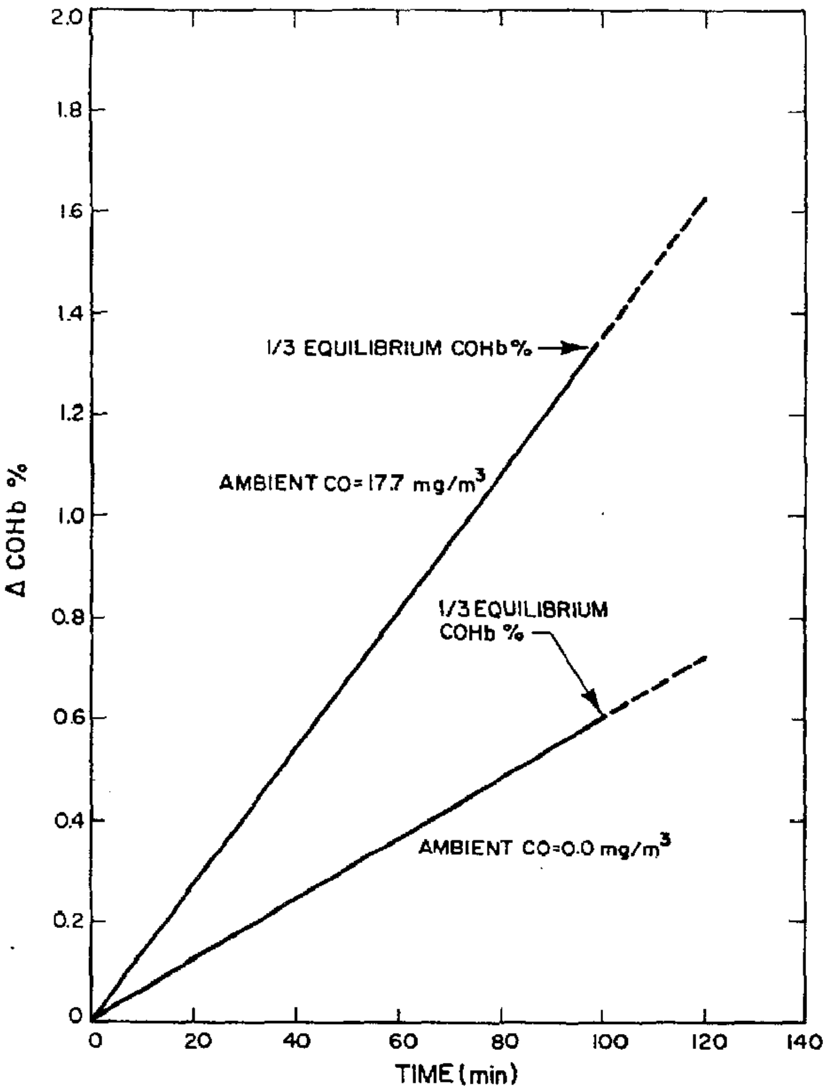

Fig 2.—Δ% COHb as a function of time for the driver of an intercity bus—"worst case."

the ambient CO was set to 0.0 mg/cu m. The second line in Fig 1 then represents the calculated effect of smoking alone. The increase is now only 0.68% saturation or less than half of the total calculated increase.

Buses

According to a US Department of Transportation Study,[8] the blower system on a bus uses 20% outside air and this results in one complete air change every 3.95 minutes. No data were given on volume or flow rates in that report. It was estimated that an intercity bus has a volume of 55.9 cu m, with a total flow rate in the ventilator system of 55.9 cu m/min. This would give an estimated air change period of five minutes rather than 3.95 minutes. Assuming the 3.95 minute value to be correct, with a volume of 55.9 cu m, the outside airflow would be 14.2 cu m/min. Using the two cases from the report cited above on buses the parameters given in the Table were set.

Figure 2 is a plot of Δ%COHb vs time for case 1 and Fig 3 is the plot for case 2. As with the calculation for automobiles, setting the ambient CO concentration at 0.0 mg/cu m shows the calculated effect of cigarettes alone. The two-hour period may be more realistic than a one-hour period for an intercity bus. However, the one third of equilibrium constraint would be reached in about 100 minutes. The similarity of Fig 1 and 2 is striking and indicates that under "worst-case" conditions there is very little difference between an automobile and a bus. The more "realistic" case gives an equilibrium COHb of only 0.44% for other than ambient CO exposure. According to these calculations for a bus, as shown in Fig 3, the effect of ambient CO exposure may be greater than that of CO from smoking. These mathematical estimates may not reflect the real-life situations, and they can be regarded only as predictions until some actual experimental data are available.

Aircraft

Using data available from a study by the federal government the following parameters were set[9]:

Ambient CO = 0.35 mg/cu m
Ventilation = 64.5 cu m/min
Minute volume = 7.43, liter
No. of persons = 112
No. of smokers = 35
No. of cigarettes/person/hr = 3.5
Av height/person = 177.8 cm
Av weight/person = 68.5 kg

Calculations for this situation are rather inconsequential except as an example. In two hours the ΔCOHb is about 0.1% of saturation and at equilibrium the COHb would be about 0.4%.

Meeting Room

The room and conditions reported by Anderson and Dalhamn[7] were used for this example.

Ambient CO = 2.27 mg/cu m and 0.0 mg/cu m
Ventilation = 8.50 cu m/min
Minute volume = 11.6 liter
No. of persons = 12
No. of smokers = 7
No. of cigarettes/person/hr = 3.5
Av height = 177.8 cm
Av weight = 68.5 kg

After one hour the ΔCOHb was calculated as 0.16% for an ambient CO of 2.27 mg/cu m. The value excluding ambient CO was calculated to be 0.10% at one hour. The equilibrium values were 0.74% (2.27 mg/cu m) and 0.47%

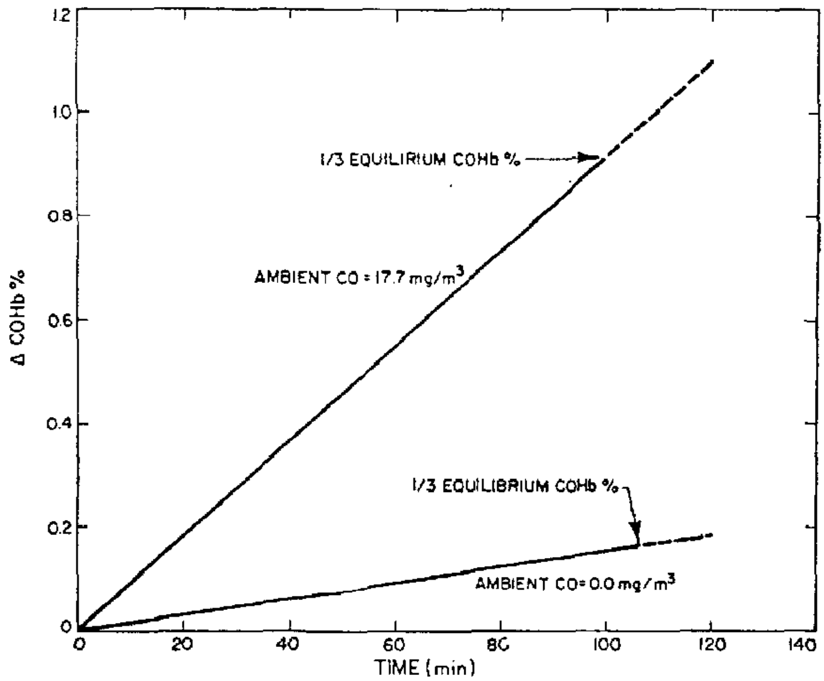

Fig 3.—Δ% COHb as a function of time for the driver of an intercity bus—"realistic case."

Measurement From Buses	Case 1	Case 2
Ambient CO (mg/cu m)	17.7 (0.0)	17.7 (0.0)
Ventilation (cu m/min)	14.2	14.2
Minute vol (1)	11.7	11.7
No. of persons	44	44
No. of smokers	43	9
No. of cigarettes/person/hr	3.5	3.5
Av height/person, cm	177.8	177.8
Av weight/person, kg	68.5	68.5

(0.0 mg/cu m). With application of the one-third criterion linearity was a valid assumption up to 100 minutes in both cases. Some further discussion of this situation is given below.

COMMENTS AND COMPARISONS WITH PUBLISHED DATA

Most empirical models for a change in COHb have dealt with the exposure of an individual to a fixed quantity of CO or to incremented concentrations.[9-12,14,16,17] No attempts have been made to isolate the various sources of CO in everyday exposure and incorporate them as parts of a model. In the model represented by equation (7), three sources of CO have been separated to permit the effects of the individual sources or any combination to be evaluated. The model to evaluate CO buildup due to smoking has been studied on a practical and theoretical basis and has been found to be a very good approximation.[3-5,13] Although the models proposed for Δ%COHb calculations have achieved a range in the region of 35,000 ppm, most studies indicate that only in quite extreme and unusual circumstances will an individual be exposed to 100 ppm or more for more than a few hours. For concentrations up to about 1,000 ppm and times up to about three hours the model of Pace et al[17] has proven to be adequate.

To prove the validity of the model presented here (equation 7) a direct comparison with observed data is available. The paper of Anderson and Dalhamn[7] gives data on a meeting room with measurements on all parameters except height and weight of the five nonsmoking subjects. The average CO for 120 minutes was cited as 4.5 ppm. Using equation (1), it was calculated as 4.6 ppm. The difference is probably within the error of measurement. The equilibrium COHb for ambient exposure may be taken as the difference between the two values cited above, or 0.3% saturation. This is the value observed in two of the nonsmokers at the beginning of the test. There were two others at 0.4% and 0.5% and a fifth at the anomolous level of 2.3%. Based solely on the calculations it would appear that linearity should hold up to about 100 minutes. All the nonsmokers, however, had an initial level in excess of one third the maximum calculated equilibrium. As a result the actual increase in either 60 or 120 minutes would have to be less than the calculated values. Since the ΔCOHb at 120 minutes was only 0.2% for smoking exposure only, little or no measurable increase should have been observed. This was in fact the case, as no increase was reported. It is also noteworthy that the measurable decrease (0.9% COHb) in the nonsmoker who started with an elevated COHb was predictable from the calculated equilibrium values.

A second comparison is available in the data given by Harke.[2] Using the data from his Table 2, the following parameters were set:

$Ci = 0.0$ and 2.27 mg/cu m
$Qi = 5.01$ and 10.12 cu m/min
$Np = 18$ persons
$Ns = 11$ smokers
$Nc = 4.75$ cigarettes/smoker/hr
$Vr = 11.6$ liter/min respiratory volume
$H = 177.8$ cm av height per person
$W = 68.5$ kg av weight per person.

No data were given on the ambient CO, so 0.0 mg/cu m and 2.27 mg/cu m were arbitrarily chosen to show only the smoking effect and to approximate the conditions of Anderson and Dalhamn.[7] From these two Ci values and the two Qi values the effect of ambient CO at 2.27 mg/cu m was 0.3% COHb at equilibrium and 0.1% ΔCOHb at two hours. Assuming the 0 mg/cu m value it was calculated that the ΔCOHb at 5.01 cu m/min should be

0.7%. Harke[2] gives 0.5 ± 0.1. For 10.12 cu m/min the calculated value was 0.4% ΔCOHb. Harke[2] gives 0.5 ± 0.1. The assumption of 0 mg/cu m is equivalent to saying that the subjects were at equilibrium with ambient CO at the beginning of the experiment.

An interesting point is that the leak rate in Harke's[2] "unventilated" room can be estimated from equation (8). This was found to be about 1.06 cu m/min, which is not far from the 1.42 cu m/min value estimated as a normal leak rate.[13]

Other comparisons can be made if it is recognized that certain published data represent only special cases of equation (7).

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Index of Gods and Hero-Persons
Hecate

What, to me,
Is Hecate?
She's cold and quiet
And makes her diet
Of souls in hell.
For quite a spell,
If I can or may,
I'd rather delay
Taking tea
With Hecate.

—Rusticatus

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